

CD61-driven stemness program in epithelial cancer

Grant Award Details

CD61-driven stemness program in epithelial cancer

Grant Type: Basic Biology V

Grant Number: RB5-06978

Project Objective: To investigate how CD61 regulates cancer stem cell fate and to understand how this pathway could be disrupted to prevent a tumor from acquiring stem-like abilities during the course of therapy.

Investigator:

Name:	David Cheresh
Institution:	University of California, San Diego
Type:	PI

Disease Focus: Cancer, Solid Tumors

Human Stem Cell Use: Cancer Stem Cell

Award Value: \$1,161,000

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 2

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Reporting Period: Year 3

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Grant Application Details

Application Title: CD61-driven stemness program in epithelial cancer

Public Abstract: Tumors contain a heterogeneous mix of cancer cells with distinct features, including subsets of particularly aggressive stem-like cells. Since a single cancer stem cell can self-renew, divide, and differentiate to reconstitute the heterogeneity of an entire tumor, the ability of one cell to evade therapy or surgical resection could lead to tumor re-growth and disease relapse.

Few, if any, individual markers have been capable of identifying cancer stem cells among distinct tumor types. It is therefore remarkable that we have detected enrichment of CD61 on stem-like cells within tumor biopsies from many different drug-resistant samples of lung, breast, pancreatic, and brain tumors from mice or humans.

CD61 promotes a stem-like reprogramming event, since ectopic expression CD61 induces stemness, including self-renewal, tumor-forming ability, and resistance to therapy. CD61 drives these behaviors by activating a signaling pathway which can be inhibited to reverse stemness and sensitize tumors to therapy.

Our project is focused on learning how CD61 drives this cancer stem cell program, and how the increase in CD61 could be prevented or reversed. If successful, our work will provide valuable new insight into a cancer stem cell program that is unexpectedly shared among a variety of solid tumor types.

Statement of Benefit to California: The American Cancer Society estimates 171,330 new cancer cases will be diagnosed in California this year, a 10th of the national total. As part of an NCI-designated comprehensive cancer, we are uniquely positioned to translate our basic science research into clinical impact for the cancer patients within our community.

From a clinical perspective, the understanding gained from our proposed studies will broadly benefit patients in California who will be diagnosed with an epithelial cancer this year, including 25,360 new breast cancer patients and 18,720 new lung cancer patients. Gaining fundamental insight into how these cancers are reprogrammed to become more stem cell-like as they acquire resistance to therapy will facilitate development of new strategies to prevent or reverse this behavior to benefit these large numbers of patients who live in California. In addition, our work will also yield new diagnostic tools that could identify which patients might respond to certain therapies.

At the basic science level, our project will also serve to elucidate the mechanisms by which cancer stem cells contribute to cancer progression and response to therapy. During the course of our project, we will be able to train more people in California to work on this cutting-edge research, and to establish a foundation for the logical design of anti-cancer therapies targeting this unique cancer stem cell population.

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